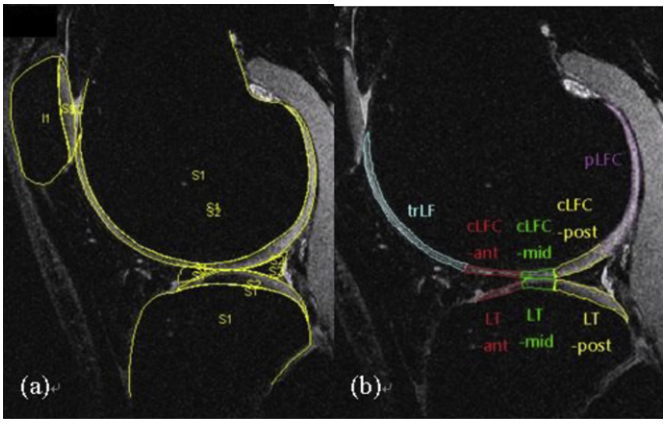
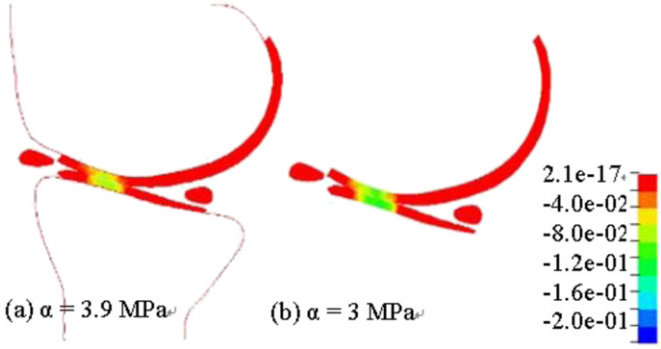
techniques such as T1ρ MRI coupled with FE analysis may allow for quantification of knee joint biomechanics as well as early detection of cartilage matrix degeneration.





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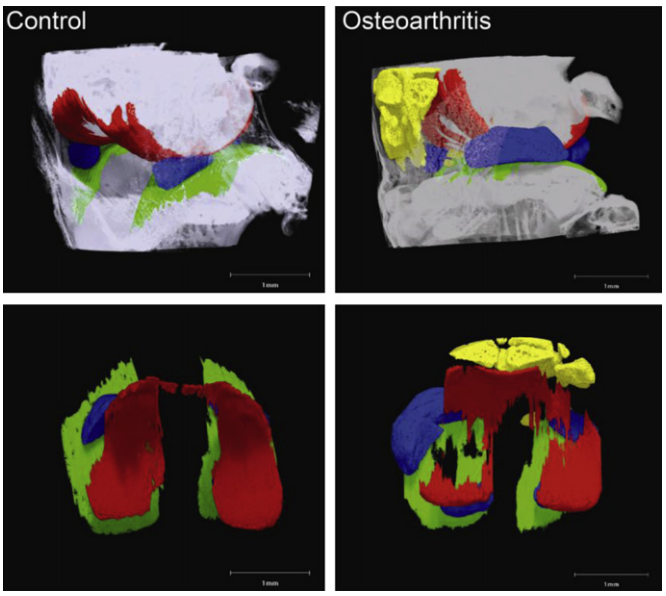
QUANTITATIVE IMAGING OF MURINE OSTEOARTHRITIC CARTILAGE BY PHASE CONTRAST MICRO-COMPUTED TOMOGRAPHY

M.Z. Ruan, B. Dawson, M.-M. Jiang, F. Gannon, M. Heggeness, B. Lee. *Baylor Coll. of Med., Houston, TX, USA*

Purpose: Mouse is an optimal model organism in which gene-environment interactions can be studied for the pathogenesis of osteoarthritis. The gold standard in arthritis research in mice is based on histopathology and immunohistochemistry, which are labor intensive, prone to sampling bias and technical variability, and limited in throughput. This study aims to develop a new technique that assesses mouse cartilage by integrating quantitative volumetric imaging techniques.
Methods: A novel mouse model of osteoarthritis was generated by cruciate ligament transection (CLT) and evaluated by histopathology and immunohistochemistry. Knee joint samples were then imaged by a novel technique that combines high resolution μCT and phase-contrast optics followed by quantitative analyses. A comparative analysis was also performed on a previously established mouse model of osteoarthritis generated by destabilization of medial meniscus (DMM).
Results: Phase contrast μCT achieved cellular resolution of chondrocytes and quantitative assessment of parameters such as articular cartilage volume and surface area. In mouse models of OA generated by either CLT or DMM, we showed that phase contrast μCT distinguished control and OA cartilage by providing quantitative measures with high reproducibility and minimal variability. Features of OA at the cellular or tissue levels could also be observed in images generated by phase contrast μCT.
Conclusions: We established an imaging technology that comprehensively assessed and quantified the 2 and 3 dimensional changes of articular cartilage. Application of this technology will facilitate the rapid and high throughput assessment of genetic and therapeutic models of OA in mice.



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HIGH RESOLUTION T1ρ MAPPING OF HUMAN KNEE CARTILAGE AT 7T

A. Singh, M. Haris, K. Cai, F. Kogan, B. Hendler, R.P. Nanga, W.R. Witschey, A. Borthakur, H. Hariharan, R. Reddy. *Univ. of Pennsylvania, Philadelphia, PA, USA*

Purpose: Purpose of the current study was to demonstrate the feasibility of a high-resolution (0.2 mm2) spin lattice relaxation time in rotating frame (T1ρ) map of in vivo human knee cartilage. Currently, T1ρ mapping of cartilage is performed on routine clinical MRI scanners (1.5 and 3T) and being used to explore early molecular changes associated with Osteoarthritis (OA). Since cartilage is a thin tissue with a thickness of 1-6 mm, a high resolution MRI is always desirable for better characterization of cartilage molecular integrity. However, resolution of low-field T1ρ maps is limited mainly due to signal-to-noise-ratio (SNR) issue. At clinical scanners, routine T1ρ mapping is performed with in plane resolution of ~0.6 mm2. Since there is an expected increase in SNR of >2 times from 3T to 7T, this increase in SNR can be used for obtaining higher resolution T1ρ mapping.
Methods: Following informed consent, four healthy volunteers (25-33 Y) underwent T1ρ MRI of knee at a high field whole body 7T scanner using a 28-channel-receiver knee coil (Quality Electrodynamics, Mayfield Village, OH). T1ρ pulse sequence consists of three parts, a B1 and B0 compensated T1ρ prepared pulse cluster followed by a chemical shift selective fat saturation pulse and a segmented radiofrequency spoiled GRE readout acquisition with centric phase encoding order.
T1ρ imaging was performed with a spin lock pulse amplitude B1sl = 500 Hz and spin lock times (TSLs) =0, 10, 20, 30, 40 ms, 3D-flash readout TR/TE =9.7/4.9 ms, flip angle =10o, FOV=140×140 mm2, matrix size =448×448, slice thickness =3 mm, number of slices = 12, number of averages = 1, number of shots =2 and a shot TR of 5s. Phase encoding direction was from R->L with resolution of 50%. Scan time for one set of T1ρ data (slices =12 and TSLs =5) was 10 minutes. Two sets of T1ρ data were acquired, one in axial orientation for patella/trochlear cartilage and other in coronal orientation for femur/tibia cartilage. For minimizing field inhomogeneity on cartilage, reference frequency and voltage were set corresponding to a small shim volume covering cartilage tissue of interest. Similarly, we acquired T1ρ data for the same volunteers and with the same sequence parameters in a 3T clinical scanner using 8-channel-receive knee coil. The T1ρ-weighted (T1ρ-W) data corresponding to different TSLs were fitted voxel-wise to mono-exponential decay expression $S(TSL) = S(0)\times\exp(-TSL/T1\rho)$ for computing T1ρ values.
Results: T1ρ signal decays mono-exponentially with increase in TSL. T1ρ values at 7T, as expected, were lower (~20%) compared to those at 3T. Despite the changes in T1 and T2 of cartilage at 7T, SNR of T1ρ-W images obtained at 7T was ~2 times higher compared to at 3T. High

resolution cartilage T1ρ maps (In plane resolution = 0.2 mm2) clearly show better classification of multiple cartilage layers at 7T compared to 3T (Fig. 1). Pixel profile of T1ρ values on the high-resolution map showed a monotonic increase from deep to superficial zone (~36 to 55 ms) at 7T while profile obtained at 3T were highly noisy (Fig. 2). These preliminary data clearly shows advantage of T1ρ mapping in term of high resolution at 7T. Evaluation of other potential advantage of T1ρ mapping at 7T requires a detailed study on patients with cartilage pathologies. Comparison of results from 7T using global and localized shim reveal that with localized shim volume around cartilage and setting of reference frequency and voltage corresponding to this volume, B0 and B1 inhomogeneity artifacts were mitigated. In this study SAR was well within scanner set limits.

Conclusions: In conclusion, increased SNR at 7T MRI can be exploited to obtain high-resolution T1ρ maps of in vivo human knee cartilage in a clinically relevant time and SAR constraints, which provides the ability to characterize cartilage molecular integrity with enhanced accuracy and precision.

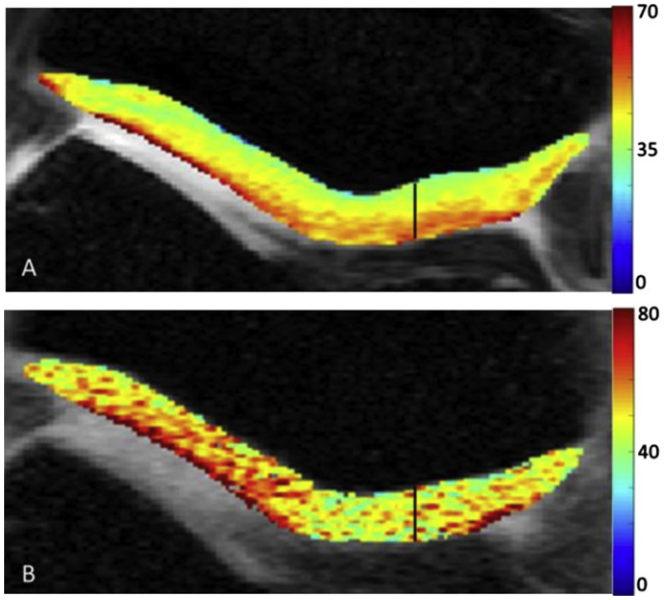

Fig. 1. A single slice high resolution T1ρ (ms) map of *in vivo* human knee patella cartilage overlaid on anatomical image from 7T (A) and 3T (B).

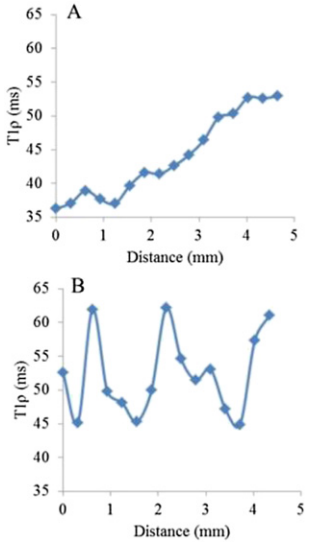

Fig. 2. Pixel profile of T1ρ values from deep to superficial zone for lines marked on Fig. 1 corresponding to 7T (A) and 3T (B).

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RELIABILITY OF A UNI-COMPARTMENTAL SCALE FOR THE RADIOGRAPHIC EVALUATION OF KNEE ARTHRITIS: DATA FROM THE MULTICENTER OSTEOARTHRITIS STUDY

L.M. Sheehy [†], T.V. Cooke [†], L.B. McLean [†], J. Niu [‡], J. Lynch [§], J. Singh [‖], N.A. Segal [¶], E. Culham [†]. [†] *Queen's Univ. Sch. of Rehabilitation Therapy, Ottawa, ON, Canada;* [‡] *Boston Univ. Sch. of Med., Boston, MA, USA;* [§] *Univ. of California at San Francisco, San Francisco, CA, USA;* [‖] *Univ. of Alabama Sch. of Med., Birmingham, AL, USA;* [¶] *Univ. of Iowa, Iowa City, IA, USA*

Purpose: Existing scales used to evaluate radiographic knee osteoarthritis (OA) lack the precision and sensitivity required to grade the severity of knee OA and detect progression. The UniCompartmental OsteoArthritis Grade (UCOAG) is a novel scale used to determine the severity of knee OA on a frontal radiograph. This scale focuses on the most-damaged tibiofemoral compartment and is associated with measures of frontal leg alignment. Four features of knee OA (joint space width, presence and extent of femoral osteophytes, presence and degree of tibial erosion and evidence of subluxation) are combined for a total score ranging from zero to 13. The purpose of this study was to assess the intra-rater reliability (one reader assesses a radiograph more than once), inter-rater reliability (more than one reader assesses the same radiograph), and test-retest reliability (one reader assesses two radiographs of the same person) of the UCOAG.

Methods: Two samples of posterior-anterior fixed-flexion knee radiographs were selected from the Multicenter Osteoarthritis Study database (NIH-funded). Potential subjects were stratified into four OA severity categories using magnetic resonance imaging (MRI). The medial tibiofemoral (TF) compartment was the more affected compartment in 70% of participants.

The first sample of 100 images was used to determine intra- and inter-rater reliability. Three readers graded the 100 images twice, two weeks apart.

A second sample of 100 radiograph pairs was used for test-retest reliability. Two radiographs of the same knee were acquired 15 or 30 months apart. Knees without any increase in cartilage damage, as determined by MRI, were chosen. One reader graded these images.

Trained readers graded the radiographs using the UCOAG scale. The most-affected TF compartment, scores for each sub-category and total score for each image were recorded.

Intraclass correlation coefficients ($ICC_{2,1}$) and Cohen's weighted kappa were performed for each type of reliability. Minimal detectable change (MDC_{90}) was calculated using test-retest reliability data.

Results: For the first sample, UCOAG grades ranged from zero to 12, with a median of four and an interquartile range (IQR) of three. ICCs for intra-rater reliability were 0.84 to 0.91. Cohen's weighted kappas were 0.65 to 0.75.

For inter-rater reliability the ICC was 0.79. Cohen's weighted kappas between pairs of readers were 0.47 to 0.61.

For the second sample, UCOAG grades ranged from zero to ten, with a median of four and IQR of four. The ICC for test-retest reliability was 0.86. Weighted kappa was 0.64. The standard error of the measurement, used to calculate the MDC_{90}, was 0.86. The MDC_{90} was 1.99. Therefore a change of two UCOAG grades would be needed to have a measurable change in OA severity.

Conclusion: The UCOAG has good to excellent intra-rater reliability, moderate to excellent inter-rater reliability and good to excellent test-retest reliability. These results are consistent with prior analyses on the reliability of the UCOAG. The UCOAG can thus be used with confidence for grading the severity of radiographic TF OA. Future research to assess the UCOAG's sensitivity to TF OA progression is needed for it to be used to assess radiographic TF OA progression in population-based studies and for monitoring the effect of treatment.

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IDENTIFICATION OF SUBCHONDRAL PROTRUSIONS BY MAGNETIC RESONANCE IMAGING: A NOVEL BIOMARKER OF JOINT DEGENERATION

A. Boyde [†], N. Jeffery [‡], V.L. Adams [‡], G. Kemp [‡], J.C. Jarvis [‡], J. Davidson [§], K. Irion [§], L.R. Ranganath [‡], J.A. Gallagher [‡]. [†] *Queen Mary Univ. of London, London, United Kingdom;* [‡] *Univ. of Liverpool, Liverpool, United Kingdom;* [§] *Royal Liverpool Univ. Hosp., Liverpool, United Kingdom*

Purpose: Subchondral protrusions were first discovered in the metacarpal condyles of Thoroughbred racehorses with palmar osteochondral